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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/349,713	07/08/1999	HERWIG BUCHHOLZ	MERCK-1900	7039

23599 7590 11/04/2004

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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT PAPER NUMBER

1617

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary****Application No.**

09/349,713

**Applicant(s)**

BUCHHOLZ ET AL.

**Examiner**

Shahnam Sharareh

**Art Unit**

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,4,5,7-10,13,14 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,7-10,13,14 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Amendment filed on August 30, 2004 has been entered. Claims 1, 4-5, 7-10, 13-14, 26 are pending. Any rejection that is not addressed here is considered obviated in view of the amendments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Double Patenting***

2. Claims 1, 4-5, 7-10, 13-14, 26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,491,948. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of pending claims are anticipated with those already patented.

Instant claim 1 encompass pharmaceutical compositions comprising isoquercitrin. Instant claim 8 is directed to formulations such as a tablet. Therefore, the instant claims are directed to oral tablets comprising isoquercitrin. The patented claims are directed to oral formulations of isoquercitrin and ascorbic acid. Accordingly, one of ordinary skill in the art in possession of the patented claims would have practiced the instant pending claims.

Applicant's agreements that the instant claims no longer recite an ascorbic acid component or other vitamins have been fully considered but are not persuasive, because it is not commensurate with the scope of the claims. The instant composition claims recite the transitional phrase "comprising." Such phrase is inclusive of any

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tertiary components including ascorbic acid. Therefore, the mere fact that ascorbic acid is no longer recited, as a second component does not exclude its use as a tertiary component in the instant compositions. Thus, Applicant's arguments are not commensurate with the scope of the claims.

***Claim Rejections - 35 USC § 103***

3. Claims 1, 4, 7-8, 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abou-Karam et al (J Nat Prod. 1992, Oct; 55(10):1525-7) in view of and Bean US Patent 4,132,782.

Abou-Karam teaches that isoquercitrin has profound activity against simplex virus. Abou-Karam also teaches suitable antiviral doses of isoquercitrin (see abstract, and page 1525-6). Abuou-Karam also elaborates that the concentrations of isoquercitrin that is required to provide its antiviral activities is about 40mcg/ml. (see page entire 1526). Abou-Karam doesn't teach the topical formulations of isoquercitrin in combination with carotenes.

Bean shows that carotene is also effective towards herpes simplex virus and can be combined with isoquercitrin for topical compositions. (see abstract, col 2, lines 10-55).

It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose. *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980). Claims that require no more than mixing together of two conventional compounds used for the same purpose would be *prima facie* obvious.

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Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to combine isoquercitrin and carotenes to formulate a topical composition with additive effects against herpes virus because both isoquercitrin and carotenes are effective against herpes virus. Furthermore, given the large range of isoquercitrin in the instant compositions, absence of showing unexpected results it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the concentrations of isoquercitrin in the final product by routine experimentations.

4. Claims 1, 4-5, 7-10, 13-14, 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abou-Karam et al (J Nat Prod. 1992, Oct;55(10):1525-7) in view of Bean US Patent 4,132,782 as applied to claims 1, 4, 7-8, 26 above, and further in view of Lanzendorfer et al WO 96/18381.

The combined teachings of Abou-Karam and Bean are described above. The combined teachings of the cited references do not explicitly teach formulation of isoquercitrin or topical formulations comprising a UV filtering agent.

Lanzendorfer is used to show that conventional nature of art in combining flavones in oral and topical compositions. Lanzendorfer discloses topical and oral flavonoid containing compositions comprising various vitamins, UVB or UVA filters and at least one flavone including isoquercitrin derivatives. Given the fact that isoquercitrin is one of the four subspecies of quercetin, the teachings of Lanzendorfer also encompass utility of isoquercitrin. Lanzendorfer also indicates antiviral activity with his composition (see abstract, page 3-5, 43, 54-60, claims 1-7, and examples, example 27 is an oral

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preparation). Lanzendorfer does not specifically teach combining isoquercitrin with ascorbic acid, carotene or other vitamins as an antiviral formulation.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to use the teachings of Lanzendorfer and modify the combination of isoquercitrin of Abou-Karma and Bean for the purposes of preparing a topical composition of isoquercitrin with a UV filter, because as taught by Lanzendorfer preparing such topical formulations of flavones well within purview of one of ordinary skill in the art, and one of ordinary skill in the art would have been motivated to formulate topical formulations to reduce systemic side effects of antivirus drugs.

Further, it would have been obvious to one of ordinary skill in the art at the time of invention to prepare such compositions in various formulations types because formulating such compositions with a new carrier system is a matter of design choice and well within the level of an ordinary artisan.

### ***Response to Arguments***

5. Applicant's arguments with respect to claims 1-10, 12-14, 26 have been considered but are moot in view of the new ground(s) of rejection. Nevertheless, Examiner would address a few issues argued by the Applicant.

As the initial matter, Examiner states that arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). (see Arguments at page 7-8). Here, Abou Karam is used

to confirm the antiviral activity of isoquercitrin against herpes simples. Bean teaches that Isoquercitrin can be combined together for antiviral activities. Thus, their combined teachings provide for all elements of the instant compositions.

Second, Applicant's arguments that the claims no longer recite the use of ascorbic acid is not persuasive, because the claims use the transitional phrases "comprising" which is an open-ended phrases. Accordingly, no element is excluded from the compositions except those recited in the claim 1.

Third, Applicant appears to argue that the teachings of Lanzendorfer are broad and not specific to provide any motivation in the art to combine its teachings with those of Bean and Abou-Karem. In response Examiner states that the teachings of Lanzendorfer merely is used to show what is known in the art about optimizing the formulation and concentrations of ingredients in topical formulations when used in combination with flavonoids. It has been long established that absence of showing an unexpected results, it is *prima facie* obvious to combine optimize concentrations of compositions that are used for their own intended use by routine experimentation. (see MPEP 2144.05-2144.06). Applicant has not provided any unexpected result is the claimed concentrations. Therefore, applicant's arguments are not found persuasive.

### **Conclusion**

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
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